Juniper Publishers
key to the Researchers

Journal of
Pharmacology & Clinical Research

Research Article
Volume 1 Issue 1 - February 2016

J of Pharmacol & Clin Res

Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial

Minati Choudhury[1]*, Raghu MG[2], Milind P Hote[2] and MV Kalaivani[1]

[1]*Department of Cardiac anesthesia, All India Institute of Medical Sciences, India*

[2]*Department of Cardiothoracic and vascular Surgery, All India Institute of Medical Sciences, India*

Submission: February 03, 2016; **Published:** February 19, 2016

***Corresponding author:** Dr. Minati Choudhury, Professor, Department of Cardiac Anaesthesia, 7th Floor, C N Centre, All India Institute of Medical Sciences, New Delhi, Tel: +91-26593831; Email: minatichoudhury2002@yahoo.co.in

Abstract

Atrial fibrillation (AF) is one of the most commonly encountered complications following coronary artery bypass grafting, whose treatment modalities are still not definite. In this prospective randomized double blind controlled trial we evaluated the adjuvant role of oral vitamin C with intravenous magnesium sulphate for the prevention of postoperative AF among the patients who underwent CABG under cardiopulmonary bypass. Group M (n=90) received4gm of intravenous magnesium sulphate just after anesthesia induction followed by 2gm daily till the 3rd postoperative day. Group MC (n=91) received a similar dose of magnesium sulphate along with oral vitamin C 2gm on the night before surgery and their after 1 gm daily till the 3rd postoperative day. We noticed a significant number of patients from Group M suffered from AF while compared to Group MC (25.56% vs 13.9%,p=0.035).Moreover, the onset of this incidence was earlier in the former group (27.92±3.65 vs 30.55±3.24 hr, p=0.04) and lasted for a longer duration. More patients from Group M while compared with Group MC (21.11% vs 7.60%, p=0.01) needed rescue drug therapy for AF management. The incidence of AF was found to be more in male sex (71.42% vs 28.58, p=0.05), diabetic patients (28.06% vs 41.71%, p=0.02), patients with ventricular dysfunction (p=0.003) and those with poor sized vessels (p=0.004).The patients with AF had a longer duration of hospital stay (p=0.01) indicating a load on hospital resources. We conclude with an appropriate dosage and regime of intravenous magnesium, incidence of AF following CABG can be reduced but its administration alone may not be sufficient for the prophylaxis. Vitamin C as an adjuvant therapy is effective in reducing the incidence of AF.

Keywords: Coronary Artery Bypass Grafting; Trial Fibrillation; Magnesium Sulphate; Vitamin C

Abbreviations

AF: Atrial Fibrillation; CABG: Coronary Artery Bypass Grafting; IV: Intra Venous; CPB: Cardio Pulmonary Bypass; ICU: Intensive Care Unit; BSA: Body Surface Area; DOE; Dyspnoea On Exertion; MI: Myocardial Infarction; DM: Diabetes Mellitus; HTN: Hypertension; FH: Family History; CCB: Calcium Channel Blocker; ACE-I: Angiotensin Enzyme Converting Inhibitor; DVD: Double Vessel Disease; TVD: Triple Vessel Disease; HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; EF; Ejection Fraction; LV: left Ventricle; LMCA: Left Main Coronary Artery; LIMA: Left Internal Mammary Artery; RCA: Right Coronary Artery.

Introduction

Atrial fibrillation (AF) is a frequent postoperative complication seen early after coronary artery bypass grafting (CABG) with a reported incidence of 20% to 50% [1]. Its onset is usually between 24 and 96 hours after surgery, with a peak incidence on the second to third postoperative day [1,2]. Atrial fibrillation potentially leads to prolonged hospitalization and significant morbidity, particularly hemodynamic deterioration and is an important risk factor for perioperative cerebrovascular accidents and perioperative myocardial infarction [3]. This subsequently leads to increase health care cost. The frequency of AF has not decreased despite recent developments in cardiac surgical technique, anesthetic management and myocardial

management; hence search for an AF prophylaxis agent is important [4]. The mechanism of development of AF in these groups of patients has not been clearly defined. Possibly it is multi factorial, and factors like advanced age, withdrawal of β blockers, inadequate atrial protection, right coronary artery disease and electrolyte imbalance particularly hypomagnesaemia have been consistently associated with postoperative AF [2,5,6]. Hypo magnesia has been reported after cardiopulmonary bypass due to hemodilution, increased urinary loss and elevated catecholamine level [7]. Recently the role of inflammation and oxidative stress for generation of AF with free radical is under scanner [8,9]. Substance modulating inflammatory pathways and those with antioxidant properties has gain importance. Ascorbic acid with its potent antioxidant properties has found to decrease the incidence of AF in postoperative patients [10]. Several pharmacologic agents have been used to prevent postoperative atrial fibrillation with varying degrees of success. Among them only β blockers and amiodarone have been shown to decrease the incidence of this event [11,12]. However these are contraindicated in many patients, needs discontinuation in many because of side effects and also their cost effectiveness has not been proved. Magnesium sulphate has been used in prophylaxis of AF, although conflicting evidence exists [13,14]. Keeping the above facts in thought we formulated this study to assess the effect and potential efficacy of oral ascorbic acid as an adjunct to magnesium in reduction of the incidence of AF in patients undergoing CABG.

Materials and Methods

Study population

The study was designed as a prospective, randomized double blind, controlled trial to determine the role of intravenous magnesium, as well as adjuvant role of oral ascorbic acid in AF prophylaxis following CABG. A total of 181 consecutive patients scheduled for elective, isolated, first time coronary artery bypass grafting between the periods of May 2008 to December 2010 were included in the study. The exclusion criteria's for the eligibility were, patients with AF, those with history of second or third degree heart block, sufferer of obstructive sleep apnoea, severe pulmonary disease, end stage renal disease, hepatic failure or ventricular dysfunction, enlarged left atrium on preoperative echocardiography, patients with pacemaker or on medication with antiarrhythmic drug therapy or with digoxin and those who had to undergo emergency CABG. The study was approved by the hospital ethics committee, and informed consent was obtained from all patients or their authorized representative.

Study design

Based on previous retrospective data from our institute patients, the incidence of AF in CABG patients treated with 2gm of magnesium sulphate during the intra opertive period and their after till the second postoperative day was found to be 25%. Anticipating a 15% less incidence in patients treated with a combination of intravenous magnesium and oral ascorbic acid compared with those treated only with the former agent, with 5%level of significance and 80% power, estimated sample size was 226 patients (113 patients in each group). However, due to time constraint we could able to enroll a total number of 181 patient in the present study. All the patients underwent the routine investigations including coronary angiography and 2-D echocardiography before the enrolment. Patients were randomly allocated to two groups by using a computer generated random number table. Patients in magnesium group (M) received 4 gram of intravenous (iv) magnesium sulphate just after anesthesia induction followed by 2 grams of this drug everyday for 3 days. Patients in the ascorbic acid group (MA) were given 2 grams of effervescent vitamin C tablets on the night before surgery, followed by 1 gm daily for 3 days after surgery in addition to magnesium therapy like group M. All the drugs were administered by a resident or a staff nurse who were not the part of monitoring or data analysis.

Anesthetic management

All the patients were managed by a single surgical, anesthetic and perfusion team. All the patients were premedicated with oral diazepam 10 mg night before and 5mg morning on the day of surgery along with intravenous morphine sulphate 0.2 mgm/kg body weight and intramuscular phenergan 25mg one hour before anesthesia induction. All of them were induced with intravenous thiopentone sodium 3-5mg/kg, fentanyl 5μgm/kg and rocuronium bromide 0.6 mg/kg body weight. The anesthesia was maintained with intermittent dose of fentanyl, midazolam and pancuronium bromide. Mechanical ventilation was achieved with a mixture of O_2: air (50:50) via Aestiva 5 (Datex-Ohmeda,UK) anesthesia machine. The tidal volume and respiratory rates were adjusted to maintain normocarbia.

Surgical procedure and postoperative period

Patients underwent CABG on standard cardiopulmonary bypass (CPB) technique with ascending aortic and right atrial double staged cannulation. Cardiac arrest was obtained and maintained by intermittent antegrade hyperkalemic blood cardioplegia. Left internal mammary artery, radial artery and reverse saphenous vein graft were used as deemed appropriate. All distal anastomoses were performed during total aortic cross clamping and proximal anastomoses were constructed with partial clamping of aorta during rewarming. The hemoglobin was maintained between 9-10 gm/dl throughout CPB and >11gm/dl during the study period. After surgery, all the patients were transferred to cardiac surgery intensive care unit (ICU).Post operative pain management was done with intravenous fentanyl till extubation and oral tramadol or ketorolac thereafter. Weaning from mechanical ventilation and catecholamine infusion was guided by institute protocol. Patients were discharged from the ICU to the nursing ward as soon as their hemodynamic and respiratory condition was stable. Continuous monitoring of vital parameters

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554

and 5 lead ECG was done by using Simens 7000 bed side monitor (Siemens, Danvers, USA) during their ICU stay and thereafter continuously during the hospital stay along with a standard 12 lead ECG examination was carried out twice daily till the time of discharge. All the patients were monitored for any new onset of atrial fibrillation starting from the onset of magnesium therapy till 7th postoperative day. AF was considered to be significant if it persisted for greater than 15 minutes and or required treatment because of hemodynamic compromise. If it occurred, the prophylaxis was considered to have failed and patient was treated as appropriate. Throughout the study duration serum potassium level of both the groups was maintained at a level of 4-4.5 meq/L. Intraoperatevely adequate death of anesthesia was maintained with the help of bispectral index monitoring and any evidence of pain was adequately treated throughout the study period.

Statistical analysis

Statistical analysis was carried out by using Stata 9.0 (College Statins,Texas, USA). Data were presented as number (%) or mean ± SD as appropriate. The univariate association between qualitative variable was evaluated using Chi square test and student t test was used for continuous variables. Bivariate, univariate and multivariate logistic regression was carried out to find the predictors of AF.The results for this were reported as odds ratio (95% confidence interval). In each of the analysis a p value of <0.05 was considered to be significant.

Results

We evaluated 181 patients undergoing CABG, with 90 patients receiving iv magnesium and the other 91 patients got both iv magnesium and oral ascorbic acid as AF prophylaxis. The first part of the study was dedicated to record the incidence of the development of atrial fibrillation at any point of time from the beginning of the case till the time of discharge of the patient and the importance of vitamin C and magnesium combination as AF prophylaxis; whereas the second part examined the predictors of AF in these group of patients, need of additional therapy for treatment of this episode and duration of ICU and hospital stay; and thereby an indirect assessment of the health care cost. Both the groups were comparable regarding their demographic profile and preoperative characteristics (Table 1). The clinical parameters and perioperative variables of the patients appear in Table 2 did not reveal any statistical between the groups. While studying the overall incidence of atrial fibrillation , the authors noted a significant number of cases from Group M suffered from this problem while compared with Group MC [23(25.56%) vs 12(13.9%), p=0.035]. The Group M patients had a early onset of AF when compared to Group MC (27.92±3.65 vs 30.55±3.24 hour, p=0.04).The AF episode lasted for 4 days in one of the patients in Group M while in none of the Group MC patients it was noted beyond 2nd post operative day (Table 3). Nineteen patients from Group M and 7 from Group MC (21.11% vs 7.69%, p=0.01) received additional therapy (amiodarone, digoxin or beta blocker) for the treatment of AF, whereas in the remaining patients in each group it resolved spontaneously [4(5.75%) vs 5(2.4%), p=0.23]. Bivariate analysis revealed that the incidence of AF is more in males (71.42% vs 28.58%, p=0.05), diabetic patients [38(26.03%) vs 16(45.71%),p=0.02], patients with ventricular dysfunction (p=0.003) and those with poor sized vessels (p=0.004), where as univariate and multivariate logistic regression analysis (odds ratio,± 95% CI, p value) showed higher incidence in patients suffering from diabetic mellitus and patients with LV dysfunction [(OR=2.39;CI 1.1to5.12;p=0.02and OR=3.53;CI 1.24 to 10.04; p=0.01 respectively. (Table 4,5). The duration of ICU stay and hospital stay was longer in patients suffered from AF while compared with the non sufferers (46.91±13.91 vs 39.41±7.37hours, p=0.00 and 8±3.17 vs 6.76± 2.56 days, p=0.01 respectively. None of these patients had any other organ dysfunction during their hospital stay.

Table 1: Demographics and preoperative profile, data expressed in mean± SD or number%. Data in parenthesis implies values in number%.

Variables	Group M(n=90)	Group MC (n=91)	P value
Age (year)	57.97±8.45	58.02±8.90	0.97
Sex (M:F)	77:13:00	81:10:00	0.48
BSA (m^2)	1.69±0.16	1.70±0.15	0.51
Weight (kg)	66.73±11.78	67.91±11.66	0.49
Height (cm)	163.5±7.8	164.20±7.54	0.53
DOE (%) 0 1 2	 59(65.56) 19(21.11) 12(13.33)	 53(58.24) 28(30.77) 10(10.99)	 0.32
Palpitation	9(10)	5(5.49)	0.25
MI	13(14.44)	8(8.79)	0.23
Smoking	27(30)	29(31.87)	0.78

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554

Alcohol	9(10)	10(10.99)	0.86
DM	31(34.44)	23(25.27)	0.17
HTN	43(47.78)	36(39.56)	0.25
Hypertriglyceridimia	11(12.22)	16(17.58)	0.31
FH	15(16.67)	12(13.19)	0.51
Obesity	12(13.33)	18(19.78)	0.24
Beta blocker	69(76.67)	70(76.92)	0.96
Nitrate	85(94.44)	83(91.21)	0.39
CCB	13(14.44)	10(10.99)	0.48
ACE-I	46(51.11)	43(47.25)	0.6
Vessel diseased DVD TVD	 19(21.11) 71(78.89)	 23(25.27) 68(74.73)	 0.57
HR (beats/min)	70.76±10.90	7.93±10.93	0.91
SBP (mmHg)	138.79±14.08	138.55±14.21	0.82
DBP (mmHg)	78.41±8.55	78.39±9.01	0.97
ECG-q wave	48(53.33)	50(54.95)	0.82
EF ≥55 36-50 ≤35	 59(65.56) 26(28.89) 5(5.56)	 52(57.14) 32(35.16) 7(7.69)	 0.53

Table 2: Clinical parameters and perioperative variables, data expressed in mean± SD or number%.

Variables	Group-M	Group-MC	P value
Atheromatous aorta	4(4.44)	6(6.59)	0.74
LV scar	19(21.11)	22(24.18)	0.62
LV function Normal Mild dysfunction Moderate dysfunction Severe dysfunction	 39(43.33) 20(22.22) 26(28.89) 5(5.56)	 38(41.76) 14(15.38) 32(35.16) 7(7.69)	 0.56
No of Vessel grafted 2 3 4 5	 8(8.89) 33(36.67) 47(52.22) 2(2.22)	 11(12.09) 34(37.36) 46(50.55) 0(0.00)	 0.6
LMCA disease	26(28.89)	26(28.57)	0.92
LIMA	88(97.78)	87(95.60)	0.68
RCA graft	72(80)	69(75.82)	0.49
End Arterectomy	37(41.11)	44(48.35)	0.32
Size of vessel (small)	2(2.22)	0(0)	0.24
Pacing	12(13.33)	16(17.58)	0.42
Duration of surgery(minute)	280.92±25.51	280.38±25.47	0.88
Aortic cross clamp time(minute)	50.51±11.78	51.18±12.37	0.7
Cardiopulmonary bypass time(minute) Chest tube drainage (ml)	 83.90±18.68 669.94±34.41	 83.73±18.59 645.82±33.32	 0.9 0.61

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554

Duration of ICU stay(hour)	41.66±10.11	40.06±8.71	0.25
Duration of ventilation(hour)	12.54±3.78	12.90±3.95	0.53
Duration of hospital stay(days)	7±2.72	6.67± 2.04	0.09

Table 3: Incidence of Atrial fibrillation in both the groups, data expressed in number %.

No of cases	Group-M	Group-MC	P value
Total Number (%)	23(25.56)	12(13.19)	0.035
Day-1	20(22.22)	12(13.19)	0.123
Day-2	5(5.56)	1(1.10)	0.118
Day-3	2(2.22)	0(0.000)	0.24
Day-4	1(1.11)	0(0.000)	0.49
Day-5	0	0	

Table 4: Bivariate analysis showing the predictors of atrial fibrillation, data expressed in number %.

Predictors	No arrhythmia (n=146)	Arrhythmia d(n=35)	P value
Age (year)	57.63(8.3)	59.54(9.88)	0.24
Sex (M:F)	124:22:00	34:01:00	0.051
HR(beats/min)	71.16(10.46)	69.54(12.49)	0.42
SBP(mmHg)	153.45	165.14	0.66
DBP(mmHg)	78.64(8.63)	77.37(10.53)	0.45
EF (%) ≥55 36-50 ≤35	 94(64.38) 42(28.77) 10(6.85)	 17(48.37) 16(45.71) 2(5.76)	0.45
DOE 0 1 2	 88(60.27) 39(26.71) 19(13.01)	 24(68.51) 8(22.86) 3(8.57)	0.7
Smoking	46(31.51)	10(28.57)	0.84
MI	16(10.96)	5(14.29)	0.58
DM	38(26.03)	16(45.71)	0.02
Alcohol	14(9.59)	5(14.29)	0.41
Hypertension	61(41.78)	18(51.43)	0.3
Hypertriglyceredimia	21(14.38)	6(17.14)	0.68
Family history	24(16.44)	3(8.57)	0.2
Obesity	26(17.81)	4(11.43)	0.36
ECG Q wave	80(54.79)	18(51.43)	0.72
LMCA disease	39(26.71)	13(37.14)	0.22
No of vessels DVD TVD	 32(21.92) 114(78.08)	 10(28.57) 25(71.43)	0.42
Aorta disease	9(6.16)	1(2.86)	0.44
LV scar	33(22.60)	8(22.86)	0.97

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554

LV function Normal Mild dysfunction Moderate dysfunction Severe dysfunction	 71(41.63) 23(15.75) 42(28.77) 10(6.85)	 6(17.14) 11(31.43) 16(45.71) 2(5.71)	 0.003
RCA graft	113(77.40)	28(80)	0.73
LIMA graft	140(95.89)	35(100)	0.22
Arteriotomy	64(43.84)	17(48.57)	0.61
Poor size vessel	0(0)	2(5.71)	0.004
Radial artery conduit	27(18.49)	9(25.71)	0.33
Pacing	21(14.38)	7(20)	0.4
Duration of ventilation(hours)	12.95±3.9	11.77±3.56	0.1
ICU stay(hours)	39.41±7.37	46.91±13.91	0
Hospital stay(days)	6.76±2.56)	8±3.17	0.01

Table 5: Univariate and multivariate logistic regression analysis showing the risk factors of atrial fibrillation

Probable risk factors	Unadjusted odds ratio (95% CI)		Adjusted odds ratio(95% CI)	
		P value		P value
Age			1.02(0.97,1.06)	0.25
Sex			4.58(0.55,37.99)	0.15
Smoking	0.86(0.38,1.95)	0.73		
Alcohol	1.57(0.52,4.69)	0.41		
DM			2.39(1.11,5.12)	0.02
Hypertension	1.47(0.45,3.32)	0.68		
MI	1.35(0.45,3.98)	0.72		
Hypertriglyceridemia	1.23(0.45,3.32)	0.68		
Family history	0.47(0.13,1.68)	0.25		
Obesity	0.59(0.19,1.83)	0.36		
LMCA disease	1.62(0.74,3.52)	0.22		
LV dysfunction Mild Moderate Severe			 3.70(1.09,12.52) 3.53(1.24,10.04) 1.44(0.23,9.00)	 0.03 0.01 0.69
SBP	0.98(0.95,1.00)	0.16		
DBP	0.98(0.94,1.02)	0.45		
ECG Q wave	0.87(0.41,1.82)	0.72		
Calcified aorta	0.44(0.54,3.65)	0.45		
LV scar	1.01(0.42,2.44)	0.97		
RCA graft	1.16(0.46,2.91	0.73		
Radial artery conduit	1.52(0.64,3.62)	0.33		
End arteriectomy	1.21(0.57,2.53)	0.61		
Pacing	1.48(0.57,3.84)	0.41		

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554

Discussion

The incidence of AF after CABG varies between 10-40% and it remains as a drain on hospital resources [1-4]. Incidence of AF in our study with the use of magnesium is 25.56% which is comparable to few of the reports in literature those used magnesium as prophylaxis. However there has been conflicting evidence regarding the prophylaxis role of magnesium in decreasing the incidence of AF after CABG. Various studies show incidence ranging from 0% to 34.5% [13,15-18]. Kohno et al. [13] in their retrospective study of 200 patients showed that postoperative 3 day magnesium infusion reduced the incidence of AF (16%) as compared to 35% in untreated group. Kaplan et al. [14] treated their patients with 3gm of magnesium sulphate during the preoperative period, day of surgery, and thereafter till the 3rd postoperative day. They noticed a 15% incidence AF in the treated group and 16% among the unnoticed ones. Fanning et al. [16] in their prospective study showed that prophylactic magnesium not only decreases the incidence, but also reduces the severity of AF after CABG. Toraman et al. [17] gave magnesium preoperatively, intraoperatively, as well as postoperatively for 4 days. Hey found that magnesium infusion dramatically decreases the incidence of AF after CABG, not only in hypomagnesemic patients, but also in patients with normal magnesium levels. The mean hour of onset of AF in their group of patients was 49.4±16.8 hour postoperatively in contrast to our result. However, Treggire-Venzi et al. and Parikka [3,18] and associates did not find any benefit from intravenous magnesium sulphate as prophylaxis on AF after CABG. A number of reasons account for this wide variation of results. Dosing and riming of magnesium administration is an important aspect. As the onset of AF after CABG is usually between 1st postoperative day to 3rd postoperative day, and hypomagnesaemia was demonstrable during this time, magnesium administration has to be such that it covers this period [5,6]. So our protocol was to administer magnesium intraoperatively and continue it till the 3rd postoperative day. Secondly, the criteria used to define the post operative AF and type of monitoring varies widely. Various studies have included arrhythmias with shorter durations, which are of no clinical significance and prophylaxis is not warranted. In our study patients were considered to be in AF,only when it is more than 15 minutes or when they develop symptoms or hemodynamic compromise to warrant treatment, thus representing the true load of patients requiring prophylaxis. In spite of so many proven reports considering the role of magnesium for postoperative arrhythmia prophylaxis, some studies had a query regarding the role of magnesium alone for the same [12,18]. This is because of the fact that post operative AF is multifactorial in origin. Oxidative stress due to surgical intervention and ischemia/reperfusion injury occurring in the myocardial tissue contributes to the development of tissue remodeling which in turn thought to be responsible for functional cardiac impairment and development of postoperative arrhythmia [19]. Vitamin C is an essential element in human body, a co factor for various enzymatic functions necessary for metabolic reactions. It is a powerful antioxidant that protects against oxidative stress produced by peroxide and free radicals [20]. The requirement of this element increases during trauma or tissue injury, reflecting an increase in its metabolism. Trauma and reperfusion injury during open heart surgery promotes the accumulation of proinflammatory cytokines responsible for oxidative stress. This subsequently affects the electrophysiological property of atrial myocyte leading to genesis of arrhythmia [10,21]. Carnes et al [10] gave supplemental ascorbic acid to patients before, and five days following CABG. They found that patients receiving ascorbic acid had a 16.3% incidence of post operative AF compared to 34.9% in controlled subjects. Eslami et al. [15] noted that combination of oral ascorbic acid with beta blockers is more effective than beta blockers alone and according to their view vitamin C has got an adjuvant role in the prevention of AF after cardioversion. Papoulidis and team [22] observed a significant difference in the overall incidence of postoperative AF in patients who received vitamin C in comparison with control group. A much lower incidence in our patients might be due to the use of magnesium sulfate along with vitamin C. In another report, after one week following cardioversion AF reoccurred in 4.5% of patients in the vitamin C group compared to 36.3% in control group [22] in our study, the time of onset of AF was not consistent with that reported by previous authors [15,21]. The height onset was 1st postoperative day (27.92±3.65hr and 28.82±3.69hr in Group M and MC respectively, we considered D-O as the day of surgery till 24 hour). While treated with antiarrhythmic group of drugs, more patients in Group MC restored back to the normal rhythm. Again more number of patients in Group M needed a rescue drug for AF management and regained back the rhythm later while compared with Group MC. These findings denotes a definite role of Vitamin C pertain to AF event. Unlike the previous reports, in none of our patients it was noted beyond 5th postoperative day. This might be due to the fact that supplementation of magnesium in both the groups had a protective role. A delayed onset, less incidence, and shorter duration of AF episode in MC Group of patients support the beneficial effect of vitamin C described in literature. The duration of ICU stay (p=0.00) and hospital stay (p=0.01) was much longer in patients who had AF. This duration required additional expenses in term of hospital charges. Another finding in our study was, though the time for ICU stay was similar, the duration of hospital stay in MC Group was shorter by one day while compared to Group M. Even if this finding was not statistically significant it was important when factor cost was calculated. The predictors for postoperative AF have not been clearly defined. Numerous factors preoperative, operative as well as postoperative have been suggested by previous experimental and clinical observations. Among them advanced age, reduced LVEF and beta blocker withdrawal has been consistently shown as a risk factor for AF following CABG. In a study by Kohno et al. [13] mean age of patients who had AF was 69 years compared

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554

to 64 years who not experience AF. They also found that 60% patients who had AF were > 70 years. Our patients belong to a relatively younger group with mean age 58 years .This could explain the absence of age as a risk factor in our study. All the patients who had AF were on beta blockers preoperatively but this finding was not statistically significant. Since none of the patients who were not on beta blockers preoperatively had AF, beta blocker withdrawal can be taken a risk factor. Smoking by causing postoperative pulmonary ateletasis and dysfunction with resultant hypoxemia as found to be a risk factor by Adams et al was not noted in our patients [23]. Most of our patients with AF were males, had ventricular dysfunction like previous authors [21]. Our study showed a statistically significant direct relation of male sex, diabetes mellitus, poor quality vessel and ventricular dysfunction.

Limitations of the study

The lack of continuous Holter monitoring may have missed some patients with AF. Since our aim was to find out clinically significant AF this might not have affected our results. As all the patients who experienced AF had preoperative beta blocker therapy, beta blocker withdrawal as AF among the patients who received vitamin C. Thirdly we could not evaluated age as a risk factor as all of our patients were < 60 year old [13].fourthly serum magnesium and vitamin C level was never monitored at any point of time to rule out a preexisting nutritional deficiency. By monitoring serum magnesium level we could have made a differentiation among the patients who had AF due to hypermagnesemia or hypomagnesemia [16]. Finally, due to a limited time frame we could not able to enroll the desired number of patients which might affect the predictors and overall incidence of AF.

Conclusion

We conclude that with an appropriate dosage and regime of intravenous magnesium, incidence of AF following CABG can be reduced but its administration alone may not be sufficient for the prophylaxis. Vitamin C as an adjuvant therapy is inexpensive and effective regime and can be considered for the prevention of AF in patients who undergoes coronary artery bypass grafting.

Acknowledgements

We thank the anesthesia residents and staff nurses who administered the drug. Our sincere thank goes to the patients who participated in this trial.

References

1. Lauer MS, Eagle KA, Buckley MJ, DeSanctis RW (1989) Atrial fibrillation following coronary artery bypass surgery. Prog Cardio vasc Dis 31: 367-378.
2. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, et al. (1996) Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. Circulation 94(3): 390-397.
3. Treggiari-Venzi MM, Waeber JL, Perneger TV, Suter PM, Adamec R, et al. (2000) Intravenous amiodarone or magnesium sulphate is not cost-beneficial prophylaxis for atrial fibrillation after coronary artery bypass surgery. Br J Anaesth 85(5): 690-695.
4. Mathew JP, Parks R, Savino JS, Friedman AS, Koch C, et al. (1996) Atrial fibrillation following coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. Multi Center Study of Perioperative Ischemia Research Group. JAMA 276(4): 300-306.
5. Satur CM, Anderson JR, Jennings A, Newton K, Martin PG, et al. (1994) Magnesium flux caused by coronary artery bypass operation: three patterns of deficiency. Ann Thorac Surg 58(6): 1674-1678.
6. Boos CJ, Lip GYH (2005) The role of inflammation in atrial fibrillation. Int J Clin Pract 59(8): 870-872.
7. Chakraborti S, Chakraborti T, Mandal M, Mandal A, Das S, et al. (2002) Protective role of magnesium in cardiovascular diseases: a review. Mol Cell Biochem 238(1-2): 163-179.
8. Engelmann MD, Svendsen JH (2005) Inflammation in the genesis and perpetuation of atrial fibrillation. Eur Heart J 26(20): 2083-2092.
9. Korantzopoulos P, Kolettis T, Siogas K, Goudevenos J (2003) Atrial fibrillation and electrical remodeling: the potential role of inflammation and oxidative stress. Med Sci Monit 9(9): RA225-RA229.
10. Carnes CA, Chung MK, Nakayama T, Baliga RS, Piao S, et al. (2001) Ascorbate attenuates atrial pacing induced peroxynitrate formation and electrical remodelling and decreases the incidence of post operative atrial fibrillation. Circ Res 89(6): E32-E38.
11. Andrews TC, Reimold SC, Berlin JA, Antman EM (1991) Prevention of supraventricular arrhythmias after coronary artery bypass surgery. A meta-analysis of randomized control trials. Circulation 84(5 Suppl): III236-244.
12. Daoud EG, Strickberger SA, Man KC, Goyal R, Deeb GM, et al. (1997) Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery. N Engl J Med 337(25): 1785-1791.
13. Kohno H, Koyanagi T, Kasegawa H, Miyazaki M (2005) Three-day magnesium administration prevents atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 79(1): 117-126.
14. Kaplan M, Kut MS, Icer UA, Demirtas MM (2003) Intravenous magnesium sulfate prophylaxis for after coronary artery bypass surgery. J Thorac Cardiovasc Surg 125(2): 344-352.
15. Eslami M, Badkoubeh RS, Mousavi M, Radmehr H, Salehi M, et al. (2007) Oral ascorbic acid in combination with beta-blockers is more effective than beta-blockers alone in the prevention of atrial fibrillation after coronary artery bypass grafting. Tex Heart Inst J 34(3): 268-274.
16. Fanning WJ, Thomas CS, Roach A, Tomichek R, Alford WC, et al. (1991) Prophylaxis of atrial fibrillation with magnesium sulfate after coronary artery bypass grafting. Ann Thorac Surg 52(3): 529-533.
17. Toraman F, Karabulut EH, Alhan HC, Dagdelen S, Tarcan S (2001) Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 72(4): 1256-1261.
18. Parikka H, Toivonen L, Pellinen T, Verkkala K, Jarvinen A, et al. (1993) The influence of intravenous magnesium sulphate on the occurrence of atrial fibrillation after coronary artery by-pass operation. Eur Heart J 14(2): 251-258.
19. Korantzopoulos P, Kolttis TM, Kountouris E, Dimitroula V, Karanikis P, et al. (2005) Oral vitamin C administration reduces early reccurence rates after electrical cardioversion of persistent atrial fibrillation and attenuates associated inflammation. Int J Cardiol 102(2): 321-326.
20. Wilson JM (2007) A day without orange juice is like an invitation to

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554

atrial fibrillation. Tex Heart Inst J 34(3): 265-267.

21. Rodrigo R, Vinay J, Castillo R, Cereceda M, Asenjo R, et al. (2010) Use of vitamin C and E as a prophylactic therapy to prevent to prevent postoperative atrial fibrillation. Int J cardiol 138(3): 221-228.

22. Papoulidis P, Ananiadou O, Chalvatzoulis E, Ampatzidou F, Koutsogiannidis C, et al. (2011) The role of oral ascorbic acid in the prevention of atrial fibrillation after elective on pump myocardial revascularization surgery-single center experience-a pilot study. Interact Cardiovasc Thorac Surg 12(2): 121-124.

23. Adams DH, Filsoufi F, Antman EM (2005) Medical management of the patients undergoing cardiac surgery. In: Zipes DP, et al. (Eds.), Braunwald's heart disease; a textbook of cardiovascular medicine. (7th edn), Elsevier Saunders, Philadelphia, USA, pp. 1993-2020.

How to cite this article: Choudhury M, Raghu M G, Milind P H, Kalaivani M V. Intravenous Magnesium Sulphate and Its Combination with Oral Vitamin C for AF Prophylaxis in Patients Undergoing Coronary Artery Bypass Surgery: A Randomized Double Blind Controlled Trial. J of Pharmacol & Clin Res. 2016; 1(1): 555554. DOI: 10.19080/JPCR.2016.01.555554